Annals of Clinical and Analytical Medicine

Original Research

Pathological factors affecting morbidity in breast cancer with modified radical mastectomy after neoadjuvant therapy

Pathological factors of modified radical mastectomy morbidity

Murat Kartal¹, Tolga Kalaycı¹, Ahmet Erkan Bilici² ¹ Department of General Surgery ² Department of Pathology, Erzurum Regional Education and Research Hospital, Erzurum, Turkey

This study was presented as a poster presentation at the 3rd National Breast Surgery Congress on May 28-29, 2021.

Abstract

Aim: The aim of this study is to investigate the pathological factors causing postoperative complications in breast cancer patients who underwent modified radical mastectomy (MRM) after neoadjuvant therapy.

Material and Methods: Breast cancer patients who underwent MRM after neoadjuvant therapy in our clinic between 2015 and 2020 were retrospectively included in the study. The relationship between pathological parameters and postoperative complications was evaluated using Mann-Whitney U tests, independent sample t-tests, and chi-square tests and p<0.05 was considered significant.

Results: There were 21 patients meeting the study criteria. The mean age of all patients was 48.76±13.98 years (range: 29-88). Morbidity developed in 7 cases (33.3%) and the average length of stay in the hospital was 11.90±4.49 days (range: 6-20). Morbidity increased in patients with advanced age (p=0.003) and cases with microcalcification (p=0.026) and neural invasion (p=0.017) in pathological evaluation, while morbidity decreased in cases with a high mean number of reactive lymph nodes (p=0.05). In addition, seroma formation was increased in patients with advanced age and microcalcification. None of the pathological factors affected hematoma formation or surgical site infection.

Discussion: According to the results of our study, we recommend harvesting reactive axillary lymph nodes as much as possible to reduce morbidity. In addition, it should be kept in mind that morbidity may increase in patients with microcalcification and neural invasion in preoperative imaging and at advanced ages.

Keywords

Advanced Age, Microcalcification, Modified Radical Mastectomy, Morbidity, Reactive Lymph Node

DOI: 10.4328/ACAM.20780 Received: 2021-07-11 Accepted: 2021-08-20 Published Online: 2021-09-14 Printed: 2021-12-01 Ann Clin Anal Med 2021;12(12):1401-1405 Corresponding Author: Murat Kartal, Erzurum Regional Education and Research Hospital, Erzurum, Turkey. E-mail: m.kartal2587@gmail.com P: +90 507 191 96 09

Corresponding Author ORCID ID: https://orcid.org/0000-0003-1396-5365

Introduction

Carcinoma of the breast is one of the most common malignancies. In light of the Cancer Statistics 2021 report of Siegel et al., 284,200 new breast cancer cases were expected to be seen in the United States. The same report also predicted that approximately 44,130 people would die due to breast cancer in the United States [1]. The treatment of breast cancer is managed with multidisciplinary approaches. These approaches include surgery, radiotherapy, chemotherapy, hormone therapy, immunotherapy, and their combinations.

Preoperative tumor staging is the most important factor in deciding on treatment. Diagnostic imaging work-up and mass biopsy play important roles in establishing a diagnosis and informing surgical decisions on the management of the primary tumor, staging of the axilla, and the sequence of therapy [2]. Once a diagnosis of breast cancer is established, the extent of disease is assessed, which, for the most part, determines whether or not preoperative (neoadjuvant) systemic therapy is indicated. For advanced-stage tumors, systemic therapy, also known as neoadjuvant treatment, is administered as the initial treatment to reduce tumor volume and will render approximately 80% of patients operable [3]. Based on the evaluation after neoadjuvant treatment, modified radical mastectomy (MRM) is one of the surgical options.

Seroma, hematoma, wound infection, flap necrosis, pain, and edema of the hand are the main complications of MRM. Postmastectomy complication rates are variable. In the study of Browne et al., the overall complication rate was 10.1% for patients undergoing mastectomy without reconstruction [4]. On the other hand, in the study by Berry et al., the total complication rate after mastectomy was 32.5% [5].

The aim of this study is to investigate the possible pathological factors increasing postoperative complications in breast cancer patients who underwent MRM after neoadjuvant therapy.

Material and Methods

Patients undergoing MRM for breast cancer after neoadjuvant therapy between 2015 and 2020 at Erzurum Regional Education and Research Hospital, Erzurum, Turkey were included in the study. Patients who were diagnosed and treated at external centers before admission to our center and patients who underwent bilateral MRM were excluded from the study.

Patients' hospital records, consultation and operation notes, pathology reports, and clinical charts were used. Each patient's demographical data (gender, age), tumor localization, pathology reports, and postoperative complications were examined. In pathology reports, hormone receptor status, lymphatic and vascular invasion status, presence of microcalcification, presence of axillary lymph nodes (reactive, metastatic, total), and lymph node ratio were investigated. The TNM stage was defined according to the American Joint Committee on Cancer (Version 8) guidelines for breast cancer. The relationships between pathological parameters and postoperative complications and their subgroups were evaluated.

Statistical Analysis

Statistical evaluations were carried out using SPSS 22.0 (IBM Corp., Armonk, NY, USA). The normality distributions of quantitative variables were checked using the Shapiro-Wilk test.

Either an independent t-test or Mann-Whitney U test was used according to the results of the Shapiro-Wilk test. The chi-square test was used to compare qualitative variables. Differences with p-values below 0.05 were considered statistically significant. Ethical approval was obtained from the Noninvasive Clinical Research Ethics Committee of Erzurum Regional Education and Research Hospital, Erzurum, Turkey (Decision Number: 2021/12-206).

Results

There were 21 patients meeting the study criteria. The mean age of all patients was 48.76±13.98 years (range: 29-88). Thirteen (61.9%) had a tumor located in the left breast. Complications in the first 30 days after surgery were defined as morbidity. Morbidity developed in 7 patients (33.3%) (seroma in 5 patients, hematoma in the axillary region in 1 patient, and wound infection in 1 patient), and the average length of stay in the hospital was 11.90±4.49 days (range: 6-20).

In the pathological examination of the patients, the mean tumor diameter was 31.23 ± 13.04 mm (range: 10-65). The most common pathological T stage was T2 at 81%, while the most

Table 1. Clinicopathological parameters of the patients

Parameters	Value or n (%)
Age (years)	48.76±13.98 (29-88)
Pathological evaluation	
Tumor location	
· Right breast	8 (38.1%)
· Left breast	13 (61.9%)
Tumor diameter (mm)	31.23±13.04 (10-65)
Lymph node parameters	
· Number of reactive lymph nodes	15.14±8.35 (3-38)
· Number of metastatic lymph nodes	2.85±3.53 (0-12)
· Number of total lymph nodes	18±7.23 (6-38)
· LNR	0.17±0.22 (0-0.7)
Pathological T stage	
· pT1	1 (4.8%)
· pT2	17 (81%)
· pT3	3 (9.5%)
· pT4	1 (4.8%)
Pathological N stage	
· pN0	10 (47.6%)
· pN1	4 (19%)
· pN2	7 (33.3%)
M stage	
· M0	15 (71.4%)
· M1	6 (28.6%)
Microcalcification positivity	3 (14.3%)
Lymphovascular invasion positivity	9 (42.9%)
Neural invasion	7 (33.3%)
Receptor positivity	
Estrogen receptor	18 (85.7%)
Progesterone receptor	18 (85.7%)
· HER2 receptor	10 (47.6%)
· p53	3 (14.3%)
Overall morbidity	7 (33.3%)
Length of hospital stay (mean, days)	11.90±4.49 (6-20)
LNR: Lymph node ratio, T: tumor, N: node, M: metastasis.	

common pathological N stage was N0 at 47.6%. On the other hand, in the evaluation of patients with advanced imaging tools, 6 patients had distant metastasis (M1 stage). There were axillary metastatic lymph nodes in 11 cases (52.4%) with a mean diameter of 2.85 ± 3.53 mm (range: 0-12). The pathological data of the patients are shown in Table 1.

Morbidity increased in patients with advanced age (p=0.003) and those with microcalcification (p=0.026) and neural invasion (p=0.017) in pathological evaluation, while morbidity decreased in cases of a high mean number of reactive lymph nodes (p=0.05). In addition, postoperative seroma after MRM affected advanced age (p=0.019) and presence of microcalcification

Table 2. Comparison of the patients according to presence of morbidity

	Morbidity	Morbidity	
Variables	positive n=7	negative n=14	р
Age (mean)	60.71	42.78	0.003*
Pathological evaluation			
Tumor location			
· Right breast	2 (25%)	6 (75%)	
· Left breast	5 (38.5%)	8 (61.5%)	0.656**
Tumor diameter (mm)	35.14	29.28	0.345*
Lymph node parameters			
· Reactive lymph nodes (mean rank)	7	13	0.05***
· Metastatic lymph nodes (mean rank)	12.71	10.14	0.400***
· Total lymph nodes (mean)	14.57	19.71	0.128*
· LNR (mean rank)	12.79	10.11	0.360***
Pathological T stage			
· pT1	0 (0%)	1 (100%)	
· pT2	6 (35.3%)	11 (64.7%)	0 100****
· pT3	0 (0%)	2 (100%)	0.199****
· pT4	1 (100%)	0 (0%)	
Pathological N stage			
· pNO	3 (30%)	7 (70%)	
· pN1	2 (50%)	2 (50%)	0.743****
· pN2	2 (28.6%)	5 (71.4%)	
M stage			
· MO	5 (33.3%)	10 (66.7%)	
· M1	2 (33.3%)	4 (66.7%)	>0.999**
Microcalcification			
· Yes	4 (22.2%)	14 (77.8%)	
· No	3 (100%)	0 (0%)	0.026**
Lymphovascular invasion			
· Yes	3 (33.3%)	6 (66.7%)	
· No	4 (33.3%)	8 (66.7%)	>0.999**
Neural invasion			
· Yes	5 (71.4%)	2 (28.6%)	
· No	2 (14.3%)	12 (85.7%)	0.017**
Receptor positivity			
· Estrogen receptor			
o Yes	7 (38.9%)	11 (61.1%)	0 531**
o No	0 (0%)	3 (100%)	0.521**
· Progesterone receptor			
o Yes	7 (38.9%)	11 (61.1%)	0.521**
o No	0 (0%)	3 (100%)	0.521**
· HER2 receptor			
o Yes	3 (30%)	7 (70%)	>0.999**
o No	4 (36.4%)	7 (63.6%)	~0'AAA
· p53			
o Yes	1 (33.3%)	2 (66.7%)	>0.999**
o No	6 (33.3%)	12 (66.7%)	
LOS (mean, days)	9.79	11.61	0.535***
LNR: Lymph node ratio, T: tumor, N: node, M:	metastasis, LOS: le	ength of stay.	

LNR: Lymph node ratio, T: tumor, N: node, M: metastasis, LOS: length of stay. *Independent t-test, **chi-square test, ***Mann-Whitney U test, ****likelihood ratio test.

Table 3. Comparison of the	patients according to presence of
seroma	

Age (mean rank)16.609.250.019'Pathological EvaluationTurnor locationVertication1 (12.5%)7 (87.5%)0.66**1 (16.0%)9 (69.2%)0.15*1 (16.0%)9 (69.2%)0.15*1 (16.0%)9 (69.2%)0.15*1 (16.0%)9 (16.2%)0.15*1 (16.0%)12.100.15*1 (16.0%)12.0%0.15*1 (16.0%)1100%)0.15*1 (16.0%)1100%)0.15*1 (17)0.0%)1100%)1 (17)0.0%)1100%)1 (17)0.0%)10.0%)1 (17)0.0%)10.0%)1 (17)0.0%)10.0%)1 (17)0.0%)10.0%)1 (17)0.0%)10.0%)1 (17)0.0%)10.0%)1 (17)0.0%)10.0%)1 (17)0.0%)10.0%)1 (17)0.0%)10.0%)1 (11)0.0%)10.0%)1 (11)0.0%)10.0%)1 (11)0.0%)10.0%)1 (11)0.0%)10.0%)1 (11)0.0%)10.0%)1 (11)0.0%)10.0%)1 (11)0.0%)10.0%)1 (11)0.0%)10.0%)1 (11)0.0%)10.0%)1 (11)0.0%)10.0%)1 (11)0.0%)10.0%)1 (11)0.0%)10.0%)1 (11)0.0%)10.0%)1 (11)0.0%)10.0%)1 (11) <th>Variables</th> <th>Seroma positive n=5</th> <th>Seroma negative n=16</th> <th>р</th>	Variables	Seroma positive n=5	Seroma negative n=16	р
Tumor locationRight1 (12.5%)7 (87.5%) 9 (69.2%) ∂_{coler}^* Right4 (30.8%)9 (69.2%) ∂_{coler}^* Tumor diameter (Mean rank)14.809.810.130*Lymph node parameters	Age (mean rank)	16.60	9.25	0.019*
Night1 (12.5%)7 (87.5%) (9(5.2%)0.60**Left4 (30.8%)9 (69.2%)0.130*Tumor diameter (Mean rank)14.809.810.130*Lymph node parameters12.190.130** Reactive (Mean rank)7.2012.190.130** Metastatic (mean rank)7.5012.090.153*• Total (mean rank)7.5012.090.153*• pT10 (0%)1 (100%)0.44*• pT24 (23.5%)13 (76.5%)0.2100%)• pT41 (100%)0 (0%)0.41***• pT41 (100%)0 (0%)0.41***• pN02 (20%)8 (80%)0.41***• pN12 (50%)2 (50%)0.41***• MA3 (20%)12 (80%)0.41***• MA2 (33.3%)4 (66.7%)0.69***• Mitro calification10 (0%)0.09**• Yes3 (100%)0 (0%)0.09***• Yes3 (22%)9 (77.8%)0.29***• No2 (14.3%)12 (85.7%)0.29***• No3 (25%)9 (75%)0.29***• No3 (25%)9 (75%)0.29***• No3 (21.4%)13 (72.9%)0.29***• Yes3 (42.9%)3 (72.9%)0.29***• No3 (27.8%)13 (72.9%)0.29***• No3 (27.8%)13 (72.9%)0.29***• No3 (27.8%)13 (72.9%)0.29***• Yes5 (27.8%)13 (72.9%)0.29***• No3 (2	Pathological Evaluation			
Left 4 (30.8%) 9 (69.2%) 0.60** Tumor diameter (Mean rank) 14.80 9.81 0.130* Lymph node parameters 0.130* 0.130* Version (Mean rank) 7.20 12.19 0.130* Metastatic (mean rank) 12.50 10.53 0.548* Total (mean rank) 7.50 12.09 0.153* LNR (mean rank) 12.80 10.44 0.495* Pathological T stage 0 0.1100% 0.44 0.495* Pathological N stage 0 1100% 0.120% 0.121*** · pN0 2 (20%) 8 (80%) 0.41**** · pN1 2 (50%) 12 (80%) 0.59*** · M0 5 (20%) 12 (80%) 0.98*** · M1 2 (33.3%) 4 (66.7%) 0.98*** · Ves 3 (100%) 0 (0%) 0.98*** · No 2 (22.%) 7 (77.8%) 0.99*** · No 3 (25%) 9 (75%) 0.28*** · Ves 3 (42.9%)	Tumor location			
Left4 (30.8%)9 (69.2%)Tumor diameter (Mean rank)14.809.810.13°Lymph node parameters0.13°0.13°Velocitie (Mean rank)7.2012.190.13°Metastatic (mean rank)12.5010.530.548°Total (mean rank)7.5012.090.15°Pathological T stage10(0%)1(100%)pT10(0%)2(100%)0.495°pT41(100%)0(0%)0(0%)pT41(100%)0(0%)0.415°**pN02(20%)8 (80%)0.415°**pN12(50%)2(50%)0.415°**Matage12 (80%)12 (80%)0.415°**Mo3 (20%)12 (80%)0.08**No3 (20%)12 (80%)0.08**Mitor calcification10.98**Vers3 (100%)0 (0%)0.08**Vers3 (100%)0 (0%)0.08**No3 (25%)9 (77.8%)0.08**Neural invasion14 (57.1%)0.99**Vers3 (42.9%)4 (57.1%)0.99**Neural invasion113 (72.2%)0.49**Neural invasion113 (72.2%)0.49**Neural invasion113 (72.2%)0.49**Neural invasion113 (72.2%)0.49**Neural invasion113 (72.2%)0.49**No0 (0%)3 (10%)3 (10%)0.49**No13 (72.2%)13 (72.9%)0.49***<	· Right	1 (12.5%)	7 (87.5%)	0 606**
Lymph node parameters· Reactive (Mean rank)7.2012.190.130'· Metastatic (mean rank)12.5010.530.548'· Total (mean rank)7.5012.090.153'· LNR (mean rank)12.8010.440.495'Pathological T stage1100%)0.10%)· pT30 (0%)2 (100%)0.111'· pT41 (100%)0 (0%)0.111'· pT41 (100%)0 (0%)0.115''· pT41 (100%)0 (0%)0.115''· pN02 (20%)8 (80%)0.15'''· pN12 (50%)2 (50%)0.15'''· M12 (33.3%)4 (66.7%)0.98'''· M12 (33.3%)4 (66.7%)0.08'''· Yes3 (100%)0 (0%)0.08'''· Yes3 (100%)0 (0%)0.08'''· Yes3 (122.2%)7 (77.8%)0.99'''· Yes3 (42.9%)4 (57.1%)0.99'''· Yes3 (42.9%)4 (57.1%)0.99'''· Yes3 (42.9%)4 (57.1%)0.41'''· Yes3 (42.9%)4 (57.1%)0.41''''· Yes3 (42.9%)4 (57.1%)0.41''''· Yes3 (42.9%)4 (57.1%)0.41''''· Yes3 (42.9%)4 (57.1%)0.41''''· Yes5 (27.8%)13 (72.2%)0.41''''''''''''''''''''''''''''''''''''	· Left	4 (30.8%)	9 (69.2%)	0.000
Reactive (Mean rank) 7.20 12.19 0.13° Metastatic (mean rank) 7.50 12.09 0.153° Total (mean rank) 7.50 12.09 0.153° LNR (mean rank) 12.80 10.44 0.495° Pathological T stage 0 1100% 0.44 0.495° pT3 0 (0%) 2 (100%) 0.212*** pP4 1 (100%) 0 (0%) 2 (100%) pT4 1 (100%) 0 (0%) 2 (100%) pN0 2 (20%) 8 (80%) 0.415*** pN1 2 (50%) 2 (50%) 0.415*** Matage 12 3 (100%) 0 (0%) 0.98** ' Yes 3 (100%) 0 (0%) 0.08** ' Yes 3 (100%) 0 (0%) 0.08** ' Yes 3 (100%) 0 (0%) 0.08** ' Yes 3 (100%) 0 (0%) 0.29** ' No 2 (22.2%) 7 (77.8%) 0.29** ' Yes 3 (42.9%) 4 (57.1%) 0.2	Tumor diameter (Mean rank)	14.80	9.81	0.130*
Metastatic (mean rank) 12.50 10.53 0.548* Total (mean rank) 7.50 12.09 0.153* LNR (mean rank) 7.50 10.44 0.495* Pathological T stage 7 0.09%) 1 (100%) pT1 0.09%) 2 (100%) 0.212*** pT4 1 (100%) 0.09%) 2 (100%) pT4 1 (100%) 0.09%) 0.415*** pN0 2 (20%) 8 (80%) 0.415*** pN1 2 (50%) 2 (50%) 0.415*** Masage 0.212(80%) 0.958** Mil 2 (33.3%) 4 (66.7%) 0.958** Mo 3 (20%) 12 (80%) 0.968** Masage 0.008** 0.999** Mo 3 (20%) 10 (68.99%) 0.908** No 3 (25%) 9 (77.8%) 0.208** Ves 3 (42.9%) 4 (57.1%) 0.280** No 3 (21.43%) 12 (85.7%) 0.249**	Lymph node parameters			
Total (mean rank) 7.50 12.09 0.153' LNR (mean rank) 12.80 10.44 0.495' Pathological T stage (1100%) 1(100%) (1100%) pT2 4(23.5%) 13.(76.5%) (212^{***}) pT4 0(0%) 2(100%) (2100%) pT4 1(100%) 0(0%) (210%) pN0 2(20%) 8.(80%) (215^{***}) pN1 2(50%) 2(50%) (215^{***}) M0 3(20%) 12.(80%) (215^{***}) M1 2(33.3%) 4.(66.7%) $(216^{**})^{**}$ No 2(11.1%) 16.(88.9%) $(299)^{**}$ Yes 3(100%) 0(0%) $(299)^{**}$ Vers 3(100%) 0(0%) $(299)^{**}$ Vers 3(100%) 0(0%) $(299)^{**}$ Vers 3(100%) 0(0%) $(299)^{**}$ Vers 3(42.9%) 4.(57.1%) $(290)^{**}$ No 2(14.3%) 12.(85.7%) $(290)^{**}$ No 0.0(%) 3(10%) $(290)^{**}$	· Reactive (Mean rank)	7.20	12.19	0.130*
LNR (mean rank)12.8010.440.495*Pathological T stagepT10 (0%)1 (100%)pT24 (23.5%)13 (76.5%)pT30 (0%)2 (100%)pT41 (100%)0 (0%)pT41 (100%)0 (0%)Pathological N stage2 (20%)8 (80%)pN02 (20%)8 (80%)0 (415***pN12 (50%)2 (50%)0 (415***Mo3 (20%)12 (80%)0.598**M12 (50%)0 (0%)0.598**M12 (22%)0 (0%)0.698**Na2 (12.2%)7 (77.8%)0.008**Vers3 (100%)0 (0%)0.008**No3 (25%)9 (75%)*0.999**No3 (25%)9 (75%)*0.999**No3 (25%)4 (57.1%)0.280**No3 (25%)4 (57.1%)0.280**No3 (25%)4 (57.1%)0.280**No3 (10%)13 (72.2%)0.49**No0 (0%)3 (10%)0.49**No3 (27.8%)13 (72.2%)0.49**No0 (0%)3 (10%)0.49**No0 (0%)3 (10%)0.49**Progesterone receptor11No3 (27.3%)8 (80%)0.29**No3 (27.3%)8 (80%)0.49**No3 (27.3%)8 (80%)0.29**No3 (27.3%)8 (80%)0.29**No3 (27.3%)8 (80%)0.29**N	· Metastatic (mean rank)	12.50	10.53	0.548*
Pathological T stage pT1 0 (0%) 1 (100%) pT2 4 (23.5%) 13 (76.5%) pT3 0 (0%) 2 (100%) pT4 1 (100%) 0 (0%) pT4 1 (100%) 2 (100%) Pathological N stage pN0 2 (20%) 8 (80%) pN1 2 (50%) 2 (50%) Mstage	· Total (mean rank)	7.50	12.09	0.153*
n pT1 0 (0%) 1 (100%) n pT2 4 (23.5%) 13 (76.5%) n pT3 0 (0%) 2 (100%) n pT4 1 (100%) 0 (0%) Pathological N stage - - n pN0 2 (20%) 8 (80%) - n pN1 2 (50%) 2 (50%) - n pN2 1 (14.3%) 6 (85.7%) - M stage - - - - M fl 2 (33.3%) 4 (66.7%) - - M fl 2 (33.3%) 0 (0%) - - Yes 3 (100%) 0 (0%) - - Yes 3 (100%) 0 (0%) - - Yes 3 (25%) 9 (75.1%) - - Vers 3 (42.9%) 4 (57.1%) - - No 2 (14.3%) 12 (85.7%) - - Vers 3 (42.9%) 4 (57.1%) - - No 0 (0%) 3 (10%)	· LNR (mean rank)	12.80	10.44	0.495*
n pT2 4 (23.5%) 13 (76.5%) 0.212*** n pT3 0 (0%) 2 (100%) 0.212*** n pT4 1 (100%) 0 (0%) 2 (100%) Pathological N stage 2 (20%) 8 (80%) 0.415*** n pN0 2 (20%) 2 (50%) 2 (50%) 0.415*** n pN2 1 (14.3%) 6 (85.7%) 0.598** M stage .	Pathological T stage			
pT3 0 (0%) 2 (100%) 0.212*** pT4 1 (100%) 0 (0%) 2 (100%) Pathological N stage 3 0 (0%) 2 (100%) 0 (0%) PNO 2 (20%) 8 (80%) 0 (0%) 0 (115***) pNO 2 (20%) 8 (80%) 0 (0415***) pN1 2 (50%) 2 (50%) 0 (0415***) Matage 3 (20%) 12 (80%) 0 (0%) M1 2 (33.3%) 4 (66.7%) 0.598** Micro calcification 3 (100%) 0 (0%) 0.098** Vers 3 (100%) 0 (0%) 0.008** Vers 3 (100%) 0 (0%) 0.008** No 2 (22.2%) 7 (77.8%) 0.008** No 3 (25%) 9 (75%) 0.308** Receptor positivity 3 (42.9%) 4 (57.1%) 0.280** No 2 (14.3%) 12 (85.7%) 0.280** No 0 (0%) 3 (10%) 0.549** Vers 5 (27.8%) 13 (72.2%) <td>· pT1</td> <td>O (O%)</td> <td>1 (100%)</td> <td></td>	· pT1	O (O%)	1 (100%)	
· pT3 0 (0%) 2 (100%) · pT4 1 (100%) 0 (0%) Pathological N stage 2 (20%) 8 (80%) · pN0 2 (20%) 8 (80%) · pN1 2 (50%) 2 (50%) · pN2 1 (14.3%) 6 (85.7%) M stage - - · M0 3 (20%) 12 (80%) 0.415*** · M1 2 (33.3%) 4 (66.7%) 0.598** · M1 2 (33.3%) 4 (66.7%) 0.608** · Yes 3 (100%) 0 (0%) - · Yes 3 (100%) 0 (0%) - - · Yes 2 (22.2%) 7 (77.8%) - - · Yes 2 (22.2%) 7 (77.8%) - - · Yes 3 (42.9%) 4 (57.1%) - - · No 2 (14.3%) 12 (85.7%) - - · Yes 5 (27.8%) 13 (72.2%) - - · Yes 5 (27.8%) 3 (10%) - -	· pT2	4 (23.5%)	13 (76.5%)	0 212***
Pathological N stage 2 (20%) 8 (80%) 2 (50%) 0 (415***) pN1 2 (50%) 2 (50%) 0 (415***) pN2 1 (14.3%) 6 (85.7%) 0.598** Mo 3 (20%) 12 (80%) 0.598** M1 2 (33.3%) 4 (66.7%) 0.598** Mirro calcification 0.008** 0.008** Vers 3 (100%) 0 (0%) 0.008** No 2 (11.1%) 16 (88.9%) 0.008** Lympho-vascular invasion 0.008** 0.008** Vers 2 (22.2%) 7 (77.8%) 0.008** No 3 (25%) 9 (75%) 0.008** No 3 (25%) 9 (75%) 0.280** No 2 (14.3%) 12 (85.7%) 0.280** Vers 3 (42.9%) 4 (57.1%) 0.280** No 2 (14.3%) 12 (85.7%) 0.280** No 0 (0%) 3 (10%) 0.59*** No 0 (0%) 3 (10%) 0.549** No	· pT3	O (O%)	2 (100%)	0.212
pN0 2 (20%) 8 (80%) 0.415*** pN1 2 (50%) 2 (50%) 0.415*** pN2 1 (14.3%) 6 (85.7%) 0.415*** M 3 (20%) 12 (80%) 0.598** M1 2 (33.3%) 4 (66.7%) 0.598** Micro calcification 2 (11.1%) 16 (88.9%) 0.008** Lympho-vascular invasion 2 (22.2%) 7 (77.8%) 0.008** Ves 2 (22.2%) 7 (77.8%) 0.999** No 3 (25%) 9 (75%) -0.99** No 3 (25%) 9 (75%) -0.99** No 3 (25%) 9 (75%) -0.280** Verral invasion 2 (14.3%) 12 (85.7%) -0.280** No 2 (14.3%) 12 (85.7%) -0.280** No 0 (0%) 3 (10%) -0.549**	· pT4	1 (100%)	O (O%)	
N1 2 (50%) 2 (50%) 0.415*** pN2 1 (14.3%) 6 (85.7%)	Pathological N stage			
N2 1 (14.3%) 6 (85.7%) M stage	· pN0	2 (20%)	8 (80%)	
M stage	· pN1	2 (50%)	2 (50%)	0.415***
M0 3 (20%) 12 (80%) 0.598** M1 2 (33.3%) 4 (66.7%) 0.598** Micro calcification 2 (3.3%) 4 (66.7%) 0.008** Micro calcification 0 (0%) 0.008** No 2 (11.1%) 16 (88.9%) 0.008** Lympho-vascular invasion 2 (22.2%) 7 (77.8%) >0.999** No 3 (25%) 9 (75%) >0.999** No 3 (25%) 9 (75%) >0.999** Versa 3 (42.9%) 4 (57.1%) _0.280** No 2 (14.3%) 12 (85.7%) 3.280** No 2 (14.3%) 13 (72.2%) _0.280** No 0 (0%) 3 (10%) ~0.59** No 0 (0%) 3 (10%) ~0.59** No 0 (0%) 3 (10%) ~0.99** No 3	· pN2	1 (14.3%)	6 (85.7%)	
M1 2 (33.3%) 4 (66.7%) 0.598** Micro calcification - - - - - - - - - - - - - 0.098** - - - - - - - - - - 0.008** - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - -	M stage			
M1 2 (33.3%) 4 (66.7%) Micro calcification 0 (0%) 0.008** No 2 (11.1%) 16 (88.9%) 0.008** Lympho-vascular invasion 2 (22.2%) 7 (77.8%) >0.999** No 3 (25%) 9 (75%) >0.999** No 3 (25%) 9 (75%) >0.999** No 3 (25%) 9 (75%) >0.280** Neural invasion 2 (14.3%) 12 (85.7%) _0280** No 2 (14.3%) 12 (85.7%) _0280** No 2 (14.3%) 13 (72.2%) _0280** No 5 (27.8%) 13 (72.2%) _0549** No 0 (0%) 3 (10%) .549** No 0 (0%) 3 (10%) .549** No 3 (27.3%) 8 (80%) .099** No 3 (27.3%) 8 (80%) .099** No 3 (27.3%) 8 (72.7%) .0549** No 3 (27.3%) 8 (80%) .099** No 3 (27.3%) 8 (72.7%) .0549** No 3 (27.3%) 8 (72.7%)	· M0	3 (20%)	12 (80%)	0 50 9**
Yes 3 (100%) 0 (0%) $\partial O08^{**}$ No 2 (11.1%) 16 (88.9%) $\partial O08^{**}$ Lympho-vascular invasion 2 (22.2%) 7 (77.8%) $\partial O999^{**}$ No 3 (25%) 9 (75%) $\partial O88^{**}$ Neural invasion 4 (57.1%) $\partial O280^{**}$ Yes 3 (42.9%) 4 (57.1%) $\partial C80^{**}$ No 2 (14.3%) 12 (85.7%) $\partial C80^{**}$ No 2 (14.3%) 13 (72.2%) $\partial C80^{**}$ No 5 (27.8%) 13 (72.2%) $\partial C99^{**}$ No 0 (0%) 3 (10%) $\partial C99^{**}$ No 3 (27.3%) 8 (80%) $\partial C99^{**}$ No 3 (27.3%) 8 (80%) $\partial C99^{**}$ No 3 (27.3%) 8 (72.7%) $\partial C99^{**}$ No 3 (27.3%) 8 (72.7%) $\partial C99^{**}$ No 3 (27.3%) 8 (72.2%) $\partial C9$	· M1	2 (33.3%)	4 (66.7%)	0.558
No 2 (11.1%) 16 (88.9%) 0.008** Lympho-vascular invasion - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - -	Micro calcification			
No 2 (11.1%) 16 (88.9%) Lympho-vascular invasion 2 (22.2%) 7 (77.8%) No 3 (25%) 9 (75%) Neural invasion 3 (25%) 9 (75%) Neural invasion 2 (11.3%) 4 (57.1%) Yes 3 (42.9%) 4 (57.1%) No 2 (14.3%) 12 (85.7%) No 2 (14.3%) 12 (85.7%) Keceptor positivity 5 (27.8%) 13 (72.2%) No 0 (0%) 3 (10%) No 3 (27.3%) 8 (80%) No 3 (27.3%) 8 (72.7%)	· Yes	3 (100%)	O (O%)	0.009**
Yes 2 (22.2%) 7 (77.8%) >0.999** No 3 (25%) 9 (75%) >0.999** Neural invasion - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - -	· No	2 (11.1%)	16 (88.9%)	0.008
No 3 (25%) 9 (75%) >0.999** Neural invasion	Lympho-vascular invasion			
No 3 (25%) 9 (75%) Neural invasion No 3 (42.9%) 4 (57.1%) 2.280** No 2 (14.3%) 12 (85.7%) 2.280** No 2 (14.3%) 12 (85.7%) 2.80** Receptor positivity 5 (27.8%) 13 (72.2%) 3.649** No 0 (0%) 3 (10%) 3.699** No 0 (0%) 3 (10%) 3.099** No 3 (27.3%) 8 (80%) 3.099** No 3 (27.3%) 8 (72.7%) 3.099** No 3 (27.3%) 8 (72.7%) 3.699** No 5 (27.8%) 13 (72.2%) 3.699** No 5 (27.8%) 13 (70.2%) 3.699** No 5 (27.8%)	· Yes	2 (22.2%)	7 (77.8%)	>0.000**
Yes 3 (42.9%) 4 (57.1%) 0.280** No 2 (14.3%) 12 (85.7%) 0.280** Receptor positivity * Estrogen receptor * o Yes 5 (27.8%) 13 (72.2%) o No 0 (0%) 3 (10%) * Progesterone receptor * o Yes 5 (27.8%) 13 (72.2%) o No 0 (0%) 3 (10%) * Progesterone receptor * o Yes 5 (27.8%) 13 (72.2%) o No 0 (0%) 3 (10%) * HER2 receptor * o Yes 2 (20%) 8 (80%) o No 3 (27.3%) 8 (72.7%) o Yes 5 (27.8%) 13 (72.2%) o Yes 5 (27.8%) 13 (72.2%) o Yes 5 (27.8%) 13 (72.2%) o Yes 5 (27.8%) 13 (70.2%)	· No	3 (25%)	9 (75%)	20.999
No 2 (14.3%) 12 (85.7%) 0.280** Receptor positivity 12 (85.7%) 12 (85.7%) 13 (72.2%) • Fstrogen receptor 5 (27.8%) 13 (72.2%) 0.549** • No 0 (0%) 3 (10%) 0.549** • Progesterone receptor - - - • Ves 5 (27.8%) 13 (72.2%) 0.549** • No 0 (0%) 3 (10%) - • Ves 5 (27.8%) 13 (72.2%) 0.549** • No 0 (0%) 3 (10%) - • HER2 receptor - - - • No 3 (27.3%) 8 (80%) - • p53 - - - • Yes 5 (27.8%) 13 (72.2%) - • p53 - - - • Ves 5 (27.8%) 13 (72.2%) - • p53 - - - • Ves 5 (27.8%) 13 (72.2%) - • No - 5 (27.8%)	Neural invasion			
No 2 (14.3%) 12 (85.7%) Receptor positivity • Estrogen receptor 5 (27.8%) 13 (72.2%)	· Yes	3 (42.9%)	4 (57.1%)	0.280**
· Estrogen receptor o Yes 5 (27.8%) 13 (72.2%) o No 0 (0%) 3 (10%) · Progesterone receptor - - o Yes 5 (27.8%) 13 (72.2%) o No 0 (0%) 3 (10%) · Progesterone receptor - - o Yes 5 (27.8%) 13 (72.2%) o No 0 (0%) 3 (10%) · HER2 receptor - - o Yes 2 (20%) 8 (80%) o No 3 (27.3%) 8 (72.7%) o P53 - - o Yes 5 (27.8%) 13 (72.2%) o No 0 (0%) 3 (10%)	· No	2 (14.3%)	12 (85.7%)	0.200
ves 5 (27.8%) 13 (72.2%)	Receptor positivity			
No O (0%) 3 (10%) 0.549** Progesterone receptor - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - -	· Estrogen receptor			
No 0 (0%) 3 (10%) Progesterone receptor - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - -	o Yes	5 (27.8%)	13 (72.2%)	0 549**
o Yes 5 (27.8%) 13 (72.2%) 0.549** o No 0 (0%) 3 (10%) 0.549** - HER2 receptor - - - o Yes 2 (20%) 8 (80%) >0.999** o No 3 (27.3%) 8 (72.7%) >0.999** o Yes 5 (27.8%) 13 (72.2%) >0.999** o Yes 5 (27.8%) 13 (72.2%) >0.549** o No 0 (0%) 3 (10%) 0.549**	o No	O (O%)	3 (10%)	0.5 15
No O (0%) 3 (10%) 0,549** • HER2 receptor - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - <t< td=""><td>· Progesterone receptor</td><td></td><td></td><td></td></t<>	· Progesterone receptor			
No 0 (0%) 3 (10%) HER2 receptor Ves 2 (20%) 8 (80%) No 3 (27.3%) 8 (72.7%) P53 Ves 5 (27.8%) 13 (72.2%) No 0 (0%) 3 (10%)	o Yes	5 (27.8%)	13 (72.2%)	0 549**
o Yes 2 (20%) 8 (80%) o No 3 (27.3%) 8 (72.7%) · p53 o Yes 5 (27.8%) 13 (72.2%) o No 0 (0%) 3 (10%)	o No	O (O%)	3 (10%)	0.5 15
o No 3 (27.3%) 8 (72.7%) • p53 o Yes 5 (27.8%) 13 (72.2%) o No 0 (0%) 3 (10%)	· HER2 receptor			
o No 3 (27.3%) 8 (72.7%) • p53	o Yes	2 (20%)	8 (80%)	>0 999**
o Yes 5 (27.8%) 13 (72.2%) o No 0 (0%) 3 (10%) 0.549**	o No	3 (27.3%)	8 (72.7%)	~0.333
o No 0 (0%) 3 (10%) 0.549**	· p53			
o No 0 (0%) 3 (10%)	o Yes	5 (27.8%)	13 (72.2%)	0 549**
LOS (mean, days) 9.70 11.41 0.603*	o No	O (O%)	3 (10%)	
	LOS (mean, days)	9.70	11.41	0.603*

LNR: Lymph Node Ratio, T: Tumor, N:node, M: Metastasis. *Mann Whitney U test, ** Chi-square test, ***Likelihood Ratio test. in the pathology specimen. Neither postoperative hematoma nor surgical site infection was affected by the parameters investigated. The comparison of the patients according to the presence of morbidity is shown in Table 2 and the comparison according to seroma is shown in Table 3.

Discussion

Breast cancer is a global health problem all over the world. In suitable cases, the main treatment is mastectomy with or without axillary lymph node dissection. However, for advancedstage diseases, the first step of treatment is chemotherapy. After the chemotherapy process, patients are mostly scheduled for MRM [6].

The rate of postoperative complications after mastectomy ranges widely from 8% to 26% [7]. The most common complications following MRM are seroma, lymphedema, infection, and wound necrosis [8]. Postoperative complications cause a prolonged hospital stay and add psychological and economic burdens for the patient. Therefore, it is important to know the factors that prevent complications. In this study, we have evaluated morbidity in a different way, aiming to show the pathological factors that prevent morbidity.

Seroma is one of the most common complications after mastectomy with an incidence of 3% to 85% [9]. The seroma prevalence in this study was 23.8%. Some authors believe that seroma occurs due to acute inflammatory exudates in response to surgical trauma and the acute phase of wound healing [10]. During dissection, some lymph pathways are opened and lymph fluid leaks out. The leaking lymph fluid accumulates in the spaces where the adhesion of the skin flaps is difficult, especially in the axilla. Generally, seroma accumulates in the first 2 weeks postoperatively and then begins to resorb after being stable in the next 2-3 weeks. The controllable predictive factors for seroma formation are still unknown. Although the results are inconsistent, some factors affecting seroma formation have been reported. Can-Özkan et al. showed in their study that no statistical correlation was found between age, tumor diameter, or number of lymph nodes removed and seroma development [11]. However, in this study, seroma after mastectomy was mostly seen at older ages and the prevalence of seroma was in keeping with the literature range.

The roles of preoperative factors like age, obesity, and hypertension in seroma formation were studied with conflicting results. In the study of Garzali and El-Yakub, patients with higher body mass index had higher risk of seroma [12]. Intraoperative factors studied include the extent of dissection and the choice of dissector. Extensive axillary dissection and the use of electrocautery for dissection have been found to be significant in the development of seroma. Postoperative factors like short duration of drainage less than 10 days and early shoulder exercise have been associated with postmastectomy seroma. On the other hand, Pan et al. showed that neither tumor diameter nor presence of axillary lymph node metastasis affected postoperative seroma, as was seen in our study [13]. Suresh et al. showed that patients older than 40 years, those with tumor sizes above 30 mm, patients with more than 5 metastatic lymph nodes harvested, and those with total lymph node count above 20 had a higher probability of seroma in their study [14]. Petrek et al. found that the number and extent of axillary lymph node involvement were the most significant factors in the causation of seroma [15]. Unlike previous studies, neither tumor size nor lymph node parameters were seen to affect seroma formation in the present report. In contrast to other studies in the English-language literature, we found that the presence of microcalcification in pathological specimens was a poor prognosis factor for seroma development after mastectomy.

Hematoma after mastectomy occurs in 2% to 10% of all mastectomy cases. Our study's hematoma rate was 4.76%. The widespread use of electronic devices has reduced the incidence of hematoma formation [16]. Seth et al. found that age difference, tumor size, tumor localization, and lymph node number had no effects on postoperative hematoma, as did the present study.

Breast surgeries are considered essentially clean surgeries and do not require antibiotic treatment. Incidence rates for postoperative wound infections are variable and range from 3% to 19% [17]. Our study's surgical site infection rate was 4.76%. Predisposing factors for infection include seroma, separation in the wound, thin skin flaps that may have limited nutrition, impaired lymphatic drainage around the axilla, advanced age, diabetes, malnutrition, and possible host defense mechanisms [18-20]. In the study conducted by Nieto et el., patients with advanced age had a higher rate of surgical site infections [21]. However, age was not a factor affecting the surgical site infection rate in our sample.

Conclusion

Complications after mastectomy are problems that every surgeon may encounter. As in our study, seroma is the most common morbidity following mastectomy. Advanced age is a poor prognosis factor for both overall morbidity and seroma formation. The presence of neural invasion and microcalcification had negative effects on overall morbidity, while the presence of microcalcification alone had a negative effect on seroma formation. However, the number of reactive lymph nodes harvested showed a protective effect on morbidity. None of the pathological factors affected hematoma formation or surgical site infection. To date, there has not been a study evaluating the relationship between pathological factors and morbidity and morbidity subgroups, and further studies with larger numbers of cases are needed.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

Funding: None

Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

References

1. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer Statistics, 2021. CA: a Cancer Journal for Clinicians. 2021;71(1):7-33.

2. Moo T-A, Sanford R, Dang C, Morrow M. Overview of breast cancer therapy. PET clinics. 2018;13(3):339-54.

3. Tryfonidis K, Senkus E, Cardoso MJ, Cardoso F. Management of locally advanced breast cancer—perspectives and future directions. Nature reviews Clinical oncology. 2015;12(3):147-62.

4. Browne JP, Jeevan R, Gulliver-Clarke C, Pereira J, Caddy CM, van der Meulen JH. The association between complications and quality of life after mastectomy and breast reconstruction for breast cancer. Cancer. 2017;123(18):3460-7.

5. Berry T, Brooks S, Sydow N, Djohan R, Nutter B, Lyons J, et al. Complication rates of radiation on tissue expander and autologous tissue breast reconstruction. Annals of surgical oncology. 2010;17(3):202-10.

 Staradub VL, Morrow M. Modified radical mastectomy with knife technique. Archives of Surgery. 2002;137(1):105-10.

7. Chandrakar N, Shinde RK. Study the early complications of modified radical mastectomy performed. International Surgery Journal. 2018;6(1):239-43.

8. Obadiel YA. Early Complications Following Modified Radical Mastectomy— Among Breast Cancer Patients Admitted to AL Gomhory Teaching Hospital, Sana'a, Yemen between Jan. 2019-Jan. 2020. Open Access Library Journal. 2020;7(12):1.

9. Kumar S, Lal B, Misra M. Post-mastectomy seroma: a new look into the aetiology of an old problem. Journal of the Royal College of Surgeons of Edinburgh. 1995;40(5):292-4.

10. AboAmra M. Seroma formation after modified radical mastectomy. Al-Azhar Assiut Medical Journal. 2017;15(4):168.

11. Can-Ozkan F, Ozkan S, Akova A. Meme kanserinde morbidite ve mortaliteyi etkileven faktörler. Göztepe Tıp Dergisi. 2007;21(2):68-71.

12. Garzali IU, El-Yakub AI. Factors affecting seroma formation after mastectomy among West African patients: a single center experience in North West Nigeria. PAMJ-Clinical Medicine. 2020;3(174):1-6.

13. Pan X-F, Huan J-L, Qin X-J. Potential risk factors for the development of seroma following mastectomy with axillary dissection. Molecular and clinical oncology. 2015;3(1):222-6.

14. Suresh B, Sachin H, Naidu M, Gopalkrishna V. A study to evaluate the factors influencing seroma formation after breast cancer surgery at tertiary care centre. International Surgery Journal. 2018;6(1):278-82.

15. Petrek JA, Peters MM, Nori S, Knauer C, Kinne DW, Rogatko A. Axillary lymphadenectomy: a prospective, randomized trial of 13 factors influencing drainage, including early or delayed arm mobilization. Archives of Surgery. 1990;125(3):378-82.

16. Vitug AF, Newman LA. Complications in breast surgery. Surgical Clinics of North America. 2007;87(2):431-51.

 Rotstein C, Ferguson R, Cummings KM, Piedmonte MR, Lucey J, Banish A. Determinants of clean surgical wound infections for breast procedures at an oncology center. Infection Control & Hospital Epidemiology. 1992;13(4):207-14.
 Gupta R, Sinnett D, Carpenter R, Preece P, Royle G. Antibiotic prophylaxis for post-operative wound infection in clean elective breast surgery. European Journal of Surgical Oncology (EJSO). 2000;26(4):363-6.

19. Brewer VH, Hahn KA, Rohrbach BW, Bell JL, Baddour LM. Risk factor analysis for breast cellulitis complicating breast conservation therapy. Clinical infectious diseases. 2000;31(3):654-9.

20. Lefebvre D, Penel N, Deberles M, Fournier C. Incidence and surgical wound infection risk factors in breast cancer surgery. Presse medicale (Paris, France: 1983). 2000;29(35):1927-32.

21. Nieto A, Lozano M, Moro M, Keller J, Carralafuente C. Determinants of wound infections after surgery for breast cancer. Zentralblatt für Gynäkologie. 2002;124(8/9):429-33.

How to cite this article:

Murat Kartal, Tolga Kalaycı, Ahmet Erkan Bilici. Pathological factors affecting morbidity in breast cancer with modified radical mastectomy after neoadjuvant therapy. Ann Clin Anal Med 2021;12(12):1401-1405